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Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Impact REPORT

ANALYSIS AND INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

CRO contribution to drug development is substantial and growing globally

New study finds clinical outsourcing associated with faster development times at comparable quality

- Since 2001, spending by drug sponsors on clinical research services has grown 15% annually, outpacing the 11% rate for overall spending on development.
- Drug sponsors have increased their reliance on contract research organizations (CROs): headcount among major CROs grew 6% annually between 2001 and 2004, while sponsor headcount remained flat.
- In 2004, leading CROs managed 23,000 phase I-IV clinical trials worldwide, monitored more than 150,000 clinical investigators, and enrolled more than 640,000 new subjects.
- According to sponsors, projects with high CRO usage stay closer to schedule: in general, high CRO usage projects are submitted more than 30 days closer to their projected submission date than are low CRO usage projects.
- Although pivotal trials involving high CRO usage tend to be larger than those with low CRO usage, they are completed faster, especially during the study close-out period.

During the past decade, pharmaceutical and biotechnology company usage of CROs in clinical research has grown steadily, motivated largely by the need to augment capacity and contain rising R&D costs. CRO usage growth also has been driven by rising volume, scope, and complexity of global clinical trial activity, and the increasing number of smaller sponsors conducting clinical research studies. Despite the growth in global clinical research outsourcing, there has been little quantitative analyses to date conducted by independent third-parties of the overall impact of outsourcing on drug development performance and capacity.

The Tufts Center for the Study of Drug Development recently conducted a comprehensive examination of CRO usage by drug sponsors. The goals of this study were (1) to quantify the impact of outsourcing on drug development performance, and (2) to determine the operating capacity contributed by leading CROs to the drug development enterprise. This *Tufts CSDD Impact Report* presents key findings from this study.

Growth in contract clinical spending is rising rapidly, outpacing overall development spending

Global Spending on Development and Clinical Services Outsourcing*

(U.S. Dollars in Billions)

	2001	2002	2003	2004	3-Yr Annualized Growth
Development Spending	$27.3	$30.1	$33.6	$37.7	11.2%
Contract Clinical Services*	$3.7	$4.3	$4.9	$5.6	15.2%

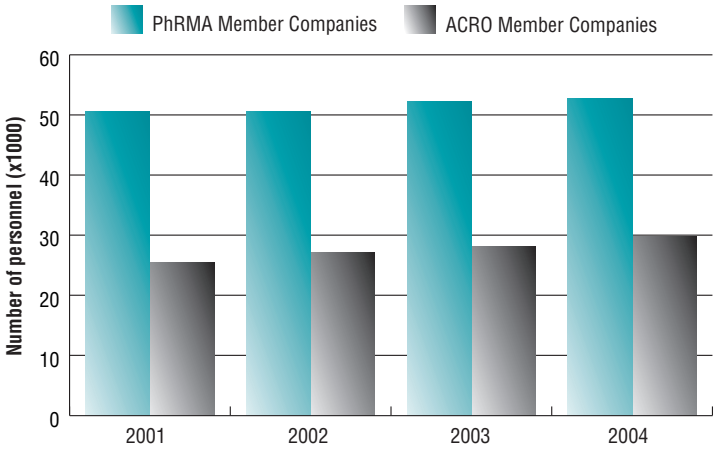
* Does not include pass-through contract clinical services (e.g., central lab fees, investigator grants)

Source: Tufts Center for the Study of Drug Development

- Global spending on contract clinical research services — not including contract lab fees and pass-through fees to investigative sites — is growing 15% annually.
- The growth in sponsor spending on outsourcing is outpacing the 11% growth in overall global development spending.
- Spending on CRO services, as a share of total global development spending, rose steadily from 13.7% in 2001 to 14.8% in 2004.

Demand for capacity, speed, and cost containment will drive strong growth in CRO usage

Global Clinical Research Personnel



Source: Tufts Center for the Study of Drug Development

- Members of the Association of Clinical Research Organizations (ACRO), who represent an estimated 70% of the total contract clinical services market, contributed nearly 30,000 clinical research personnel in 2004, up from 25,439 in 2001, a 5.5% annual growth rate.
- During the same period, sponsor head count growth has been flat while volume, scope, and complexity of development programs have been rising.
- An increasing number of small- and mid-sized companies — typically higher users of CRO services — are moving products from preclinical into clinical research programs.

The role of CROs in the clinical research enterprise is substantial

Clinical Study Activity Managed Worldwide by Major CROs

	2001	2002	2003	2004
Total Phase I-IV Studies	19,847	20,927	21,128	22,676
Total Phase I-IV Investigators	147,684	126,876	161,014	152,066
Total New Phase I-IV Patients Enrolled*	571,001	554,092	507,231	642,894

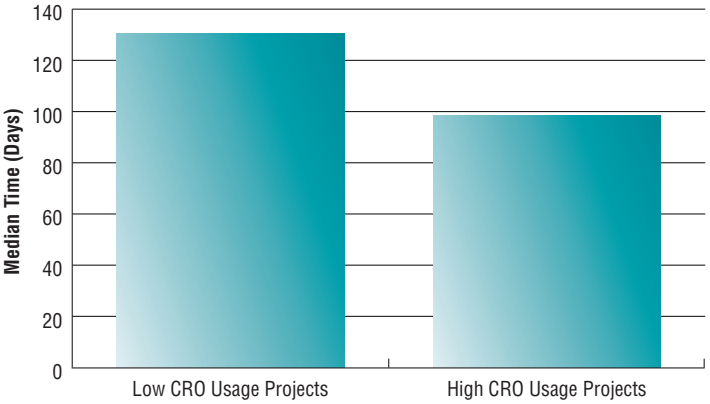
* Does not include study volunteers already participating in trials initiated in prior years

Source: Tufts Center for the Study of Drug Development

- In 2004, ACRO member companies provided services to support nearly 23,000 phase I-IV studies worldwide.
- CROs monitored substantial numbers of investigative sites and study volunteers in 2004:
  - ACRO members report identifying, selecting, and monitoring more than 150,000 clinical investigators.
  - ACRO members enrolled more than 640,000 new study volunteers in phase I-IV clinical trials.

CRO projects tend to be larger, but are more likely to be completed closer to projected timeframes

Days Actual Submission Exceeded Projected Submission Date

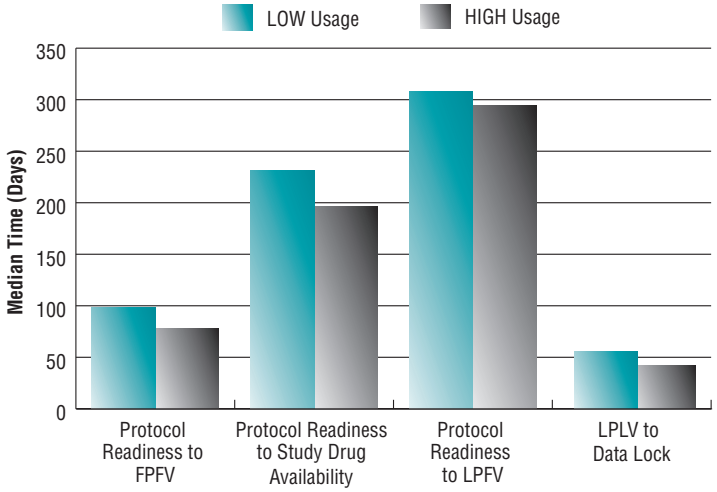


Source: Tufts Center for the Study of Drug Development

- Submissions involving high CRO usage tend to involve larger numbers of investigative sites and study volunteers than low CRO usage projects.
- High CRO usage projects, however, were typically submitted more than 30 days closer to their projected submission dates than were low CRO usage projects.
  - Median time from projected to actual submission date for low CRO usage projects was 130.5 days.
  - Median time for high CRO usage projects was 98.3 days.

CRO usage is associated with faster development times

Pivotal Trial Milestones



Source: Tufts Center for the Study of Drug Development

- Across the continuum of study conduct activities, high CRO usage projects tend to be completed faster, most notably during the study close-out period.
- Median time to final database lock is significantly faster — by two weeks on average — for projects in which a majority of the work is managed by contract service providers.
- Pivotal trials involving high CRO usage also tend to involve larger numbers of sites and volunteers.

Sponsors report comparable performance quality between high and low CRO usage projects

Case Report Form Queries/Page Screen

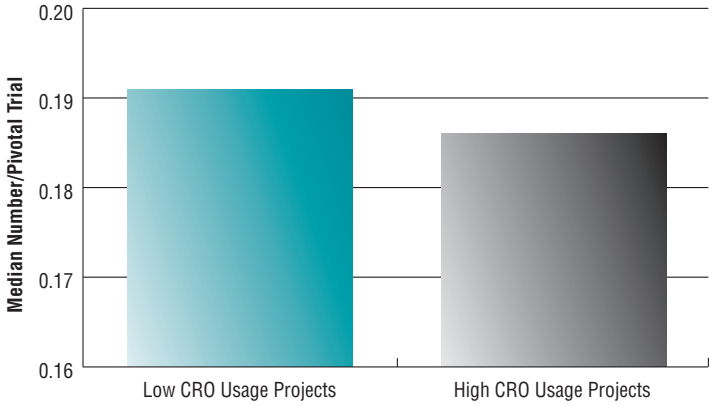


Chart shows relative rate of data collection errors

Source: Tufts Center for the Study of Drug Development

- While CRO usage is associated with faster development speed, performance quality is comparable between low and high CRO users.
- No statistically significant differences between low and high CRO usage were found when comparing queries per page screen and when comparing time from NDA submission to approval.
- There was no difference in investigative site compliance with good clinical practice guidelines between high and low CRO usage projects.

How the study was conducted

Beginning in early 2005, Tufts CSDD conducted a comprehensive study to quantify the impact of CRO usage on development performance and determine the capacity contributed by leading CROs to the drug development enterprise. Tufts CSDD conducted 31 interviews with pharmaceutical and biotechnology companies of varying sizes, gathered data from 16 sponsors on 79 NDA and 4 BLA submissions made since the year 2000, and conducted a survey among ACRO member organizations. Surveyed sponsor companies were representative of broad levels of R&D spending: (a) Five top-tier companies spending in excess of $500 million each on R&D in 2004; (b) Seven mid-tier companies spending between $100 million and $500 million each on R&D in 2004; and (c) Four third-tier companies spending less than $100 million each on R&D in 2004.

For the purpose of this study, **low CRO usage** is defined as drug sponsors spending less than 40% of their total clinical program budget on CRO services; **high CRO usage** is defined as drug sponsors spending more than 60% of their total budget on CRO services. Of the 83 NDAs/BLAs evaluated, 52 were included in the low usage group and 31 were included in the high usage group. NDA/BLAs in both groups are diverse and representative of therapeutic areas in the overall development pipeline. For the capacity impact analysis, 10 ACRO member companies provided data on their headcount, financials, and clinical research activity between 2000 and 2005. A listing of ACRO members is available at www.acrohealth.org.

Note: The analysis summarized in this *Tufts CSDD Impact Report* did not measure the impact of CRO usage on drug development economics, which will be the focus of an upcoming Tufts CSDD study.

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Definition of terms

BLA — Biologics License Application. An application to FDA for a license to market a new biological product.

CRO — Contract Research Organization. Companies contracted by pharmaceutical, biotechnology, or medical device sponsors to perform various discovery and development tasks.

FPFV – First patient, first visit; **LPFV** – Last patient, first visit; **LPLV** – Last patient, last visit.

NDA — New drug application. An application to FDA to market a new drug in the U.S.

About the Tufts Center for the Study of Drug Development

The Tufts Center for the Study of Drug Development at Tufts University provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Tufts CSDD conducts a wide range of in-depth analyses on pharmaceutical issues and, in addition, hosts symposia, workshops, and public forums on related topics.

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